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10/552,219	06/29/2006	Claudia Scharer-Brodbeck	27656/41464	6786

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EXAMINER	
JOIKE, MICHELE K	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
06/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,219	SCHARER-BRODBECK, CLAUDIA	
	Examiner	Art Unit	
	MICHELE K. JOIKE	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed March 30, 2009. Claims 1-11, 13-17 and 19-33 are pending, with claims 1-11, 13-17, 22-28 and 31-33 under consideration. Any rejection of record in the previous Office Action, mailed October 30, 2008 that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13-17 and 22-28 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Additionally, new claims 31-33 are added to the rejection. The claims stand/are rejected for the following reasons.

The term "suitable" in claim 1 is a relative term which renders the claim indefinite. The term "suitable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In claims 6, 7, 14 and 24, a "unique recognition site" is claimed. It is unclear what makes the recognition site unique.

Claim 8 is still confusing because it appears that the gamma subunit is being substituted for by an antibody, however, using an antibody in the method if claim 1 is confusing since the gamma subunit still needs to be present to perform the method steps.

Claim 9 is confusing because the claim states that the first DNA sequence of the target vector replaces at least one CDR region of the antibody, however, it appears from claim 1 that the toxin is to be replaced. Since it is unclear where the antibody is present, this also makes this claim and claims 10, 25 and 26 confusing, as well.

Response to Arguments Concerning Claim Rejections – 35 USC § 112 (2)

Applicant's arguments filed March 30, 2009 have been fully considered but they are not persuasive.

The following grounds of traversal are presented:

"Suitable" means "appropriate for", and "suitable cells" are capable of allowing homologous recombination and are sensitive to the gamma toxin. "Suitable conditions" refer to conditions which allow the chosen cells to grow, multiply, and perform homologous recombination and express gamma toxin when no homologous recombination takes place.

Unique recognition site is a single restriction site that a specific restriction enzyme will cut only once in a given DNA sequence.

Applicant's arguments have not been found persuasive for the following reasons.

"Suitable" is not defined by the specification, therefore, there is no guidance about what cells would be suitable, other than yeast cells that are capable of allowing homologous recombination and are sensitive to the gamma toxin. However, the specification does not teach that these characteristics are what make a yeast cell "suitable", and what other characteristics would also make the yeast cell suitable. One of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The same is true for "suitable conditions". There is no definition in the specification, and unless one of skill in the art what yeast cell was being used, it would be unclear what conditions for that cell are suitable.

In claim 6, "at least one recognition site for a restriction enzyme" is claimed. Applicants are arguing that a unique recognition site is a single restriction site; however, this contradicts the language in claim 6, since more than one unique recognition site can exist for the specific restriction enzyme.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 13-17, 24 and 27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Meinhardt et al in view of Butler et al, and in further view of US 6,410,271. This rejection is maintained for reasons of record. New claims 31 and 32 are added. The second plasmid taught by Meinhardt et al encodes more than two protein regions, an aminoglycoside phosphotransferase, a LEU2 marker, and a gene encoding for β-lactamase.

Claims 22 and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Meinhardt et al, Butler et al and US 6,410,271 as applied to claims 1-7, 13-16, 24 and 27 above, and further in view of Monschau et al. This rejection is maintained for reasons of record.

Claim 28 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Meinhardt et al, Butler et al and US 6,410,271 as applied to claims 1-7, 13-16, 24 and 27 above, and further in view of Jirholt et al. This rejection is maintained for reasons of record. New claim 33 is added to the rejection. US 6,410,271 teaching a methods for generating highly diverse libraries of expression vectors encoding fusion proteins, such as single-chain antibodies, via homologous recombination in yeast, and Jirholt et al teach libraries containing CDRs.

Response to Arguments Concerning Claim Rejections – 35 USC § 103 (a)

Applicant's arguments filed March 30, 2009 have been fully considered but they are not persuasive.

The following grounds of traversal are presented:

None of the art teaches use of the gamma toxin gene as a negative selection marker, or cell lines susceptible to gamma toxin effects for homologous recombination. In particular, Meinhardt teaches that the selection markers are the donor sequences and integrated into the target sequence, not the target DNA sequence. Also, the method in Meinhardt is typically not useful for generating a randomized library with the use of selection markers as donor sequences. Lastly, Meinhardt uses cells that are resistant to gamma toxin gene effects.

Butler does not teach that gamma toxin is useful as a negative selection marker which is removed by homologous recombination.

US 6,410,271 does not teach a useful negative selection system using gamma toxin as the negative selection marker for constructing a randomized library.

Applicant's arguments have not been found persuasive for the following reasons.

In the claims, the gamma toxin has been replaced by a donor sequence. In Meinhardt, integration of the LEU2 and *aph* genes disrupts the killer toxin. Therefore the procedure of having the killer toxin disrupted by integration is the same. See figure 1. Butler is the reference that teaches the gamma toxin as a negative selection marker, and use of cells that are susceptible to gamma toxin. The method using homologous recombination for integration to disrupt a killer toxin is taught by Meinhardt, as discussed above. US 6,410,271 is the reference that teaches a method for generating highly diverse libraries of expression

vectors encoding fusion proteins, such as single-chain antibodies, via homologous recombination in yeast. Combined, they teach the claimed method.

Allowable Subject Matter

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

Michele K. Joike
Examiner
Art Unit 1636